A206 SKEWED X CHROMOSOME INACTIVATION IN RHEUMATOID ARTHRITIS WOMEN

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Background and objectives It has long been recognised that women have a greater prevalence of autoimmune diseases. Rheumatoid arthritis (RA) does not escape this rule with a women:men ratio of 3:1.

X chromosome inactivation (XCI) is a dosage compensation mechanism used by mammals to ensure that XX females and XY males equalise X chromosome gene expression. As a consequence, females are a mosaic of two cell lines, one expressing maternal X-linked and the other expressing paternal X-linked genes with a ratio close to 50:50 when XCI is random.

However skewing, defined as a deviation from the 50:50 ratio has been described in females with autoimmune thyroid diseases, scleroderma and juvenile idiopathic arthritis (for review[1]). The aim of the current study is to test whether women with RA also have a skewed XCI.

Methods The highly polymorphic CAG repeat on the first exon of the androgen receptor gene was genotyped, as described elsewhere[2] to determine XCI bias in 84 women with RA and 100 healthy women.

Results A total of 54 patients and 69 controls were informative for androgen receptor polymorphism. Among them 31.5% of women with RA (17/54) had a skewed XCI (≥80:20) compared to only 17.4% of healthy women (12/69). Only extreme skewing was statistically significant with 18.5% of patients following this pattern and 2.9% of controls (p=0.004).

Conclusions Our preliminary data indicate that skewed XCI may be a risk factor for the occurrence of RA in women. Further studies need to be done to analyse whether women who have a skewed pattern have less genetic susceptibilities (shared epitope) or less specific autoantibodies (anti-CCP) as their risk factor is X chromosome linked.

REFERENCE

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